

Muscular-Skeletal Disorders – Research on Methods

PMS70

A COMPARISON OF NON-RESPONDER IMPUTATION AND LAST-OBSERVATION-CARRIED-FORWARD ANALYSIS METHODS IN RHEUMATOID ARTHRITIS CLINICAL TRIALS

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OBJECTIVES: To highlight the importance and impact of imputation approach used in reporting rheumatoid arthritis (RA) clinical trial results when data are analyzed using non-responder imputation (NRI) versus last observation carried forward (LOCF). **METHODS:** Non-responder imputation is a conservative analysis method in which participant dropouts are assumed to be non-responders regardless of actual response status at the time of dropout. Last observation carried forward is an analysis method in which the last measured value of a variable, such as treatment response, is carried forward and assumed to be valid for a future point of analysis. Results at 52 weeks from the PREMIER trial, a double-blind, randomized trial in adult patients with early RA (<3 years) that compared among adalimumab plus methotrexate (ADA+MTX) and monotherapies with either drug were compared using NRI and LOCF analyses. Outcome measures presented here are American College of Rheumatology (ACR) 50%, and 70% responses, and remission based on 28-joint Disease Activity Score (DAS28<2.6). **RESULTS:** In the ADA+MTX treatment group, outcome measures calculated using NRI and LOCF, respectively, were 62% and 68% for ACR50, 46% and 48% for ACR70, and 43% and 47% for remission. In the MTX-monotherapy group, NRI and LOCF values, respectively, were 46% and 49% for ACR50, 28% and 29% for ACR70, and 21% and 22% for DAS28 <2.6. For all outcome measures, the estimate of drug effect was lesser when using NRI analysis compared with LOCF analysis. **CONCLUSIONS:** Non-responder imputation analyses tend to result in more conservative estimates of drug effect on outcome measures than LOCF analyses. In trials in which there are high numbers of participant dropouts, the difference in results using NRI versus LOCF could be substantial. Thus, caution is warranted in comparisons of results across clinical trials using these different imputation methods.

PMS71

COMPARISON OF PROPENSITY SCORE MATCHING AND INSTRUMENTAL VARIABLE METHODS WHEN ESTIMATING HEALTH CARE COSTS OF RHEUMATOID ARTHRITIS PATIENTS

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OBJECTIVES: To compare the two risk adjustment models when estimating health-care costs of rheumatoid arthritis (RA) patients. **METHODS:** Continuously eligible adult patients with confirmed diagnoses of RA between June 2004 and June 2009 were included. Patients were new to tumor necrosis factor (TNF) therapy and subsequently either switched to another anti-TNF or escalated their dose. The difference in total health care costs and RA-related health care costs between switchers and escalators 1 year after the switch/escalation were estimated using the propensity score matching and instrumental variable methods. When using propensity score matching, the differences in patient, clinical, cost and utilization characteristics during the baseline period were controlled. When using the instrumental variable method, patients' copayment, distance from patient to provider, and doctors' prescribing patterns were used as instruments to estimate the outcomes, while other differences in patient and clinical characteristics were controlled as well. **RESULTS:** After risk adjustment using propensity score matching, the difference between switchers and escalators is \$648 in total healthcare costs, and \$245 in RA-related health care costs. After using the instrumental variable method, the difference between switchers and escalators is \$2054 in total health care costs and \$2809 in RA-related health care costs. **CONCLUSIONS:** After adjusting for patient, clinical and demographic characteristics, the choice of risk adjustment method affected the results. In this study, the cost burden is higher for switchers when using the instrumental variable method as the risk adjustment technique.

PMS72

SUITABILITY OF THE EFFICIENCY FRONTIER APPROACH FOR THE EVALUATION OF BIOLOGICAL AGENTS IN THE TREATMENT OF EARLY RHEUMATOID ARTHRITIS

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OBJECTIVES: The three most important biological agents adalimumab, etanercept and infliximab caused €940mn drug expenditure at a 23% annual growth rate for the German Statutory Health Insurance funds in 2009. The objective of this analysis is to test the suitability of IQWiG's efficiency frontier (EF) method for pharmacoeconomic analysis of biological agents in the treatment of early rheumatoid arthritis. **METHODS:** We apply simplified versions of the EF to infliximab. Effectiveness analysis is based on the two year findings of the BeSt trial. It was identified as the only trial to compare an active infliximab strategy to active conventional strategies including multiple disease-modifying anti-rheumatic drugs (DMARDs). In the first scenario, the analysis is conducted for the complete patient base. In the second scenario, the evaluation is limited to patients, who are resistant to conventional DMARD therapy. **RESULTS:** For the first scenario, effectiveness was measured in terms of patient response defined as a sustained DAS₄₄ score ≤2.4 after two years. The EF was constructed with the best conventional alternatives, methotrexate monotherapy and initial combination therapy with methotrexate, sulfasalazine and prednisone. They achieved 33% and 58% response at €230 and €790 cumulative expenditure. Infliximab was superior in patient response with 72% but caused

360,640 cumulative drug costs. IQWiG's approach yields inefficiency of infliximab since it is located to the right of the EF. In the second scenario, infliximab is not comparable to conventional DMARDs with the EF approach. **CONCLUSIONS:** Our analysis calls for cautious application of the EF method. Depending on the setup, the EF may fail to recognize the value of highly innovative but expensive drugs for a specific patient subgroup. In the case of missing conventional alternatives, the EF yields no global measure of efficiency for comparisons across indications. Therefore, complementary methods like IQWiG's budget impact analysis are required.

PMS73

PATIENT-CENTRIC OBSERVATIONAL STUDY ON CORRELATES OF INTENT TO PERSIST WITH TREATMENT: A REGRESSION MODEL IN OSTEOPOROSIS

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OBJECTIVES: To assess the relationship between intent to persist (ITP) and reported compliance (RC) with osteoporosis treatment versus treatment satisfaction and its predictors. Increased persistence has been linked to improved general health. **METHODS:** An online survey was administered in November 2010 to 50 US MediGuard.org community members taking at least one osteoporosis medication. Survey items included the Treatment Satisfaction Questionnaire for Medication (TSQM) with 14 items across 4 domains [effectiveness (EFF), side effects (SE), convenience (CON), global satisfaction (GS)] and covariates such as treatment cost (TCOST) and medication knowledge (KNO). Using linear regression, we assessed GS as a predictor of ITP and RC. We also explored the extent to which EFF, SE, CON, TCOST and KNO each explained GS. The Adjusted Goodness of Fit Index (AGFI) provided a measure of model fit. **RESULTS:** The tested regression model adjusting for interaction between ITP and RC was highly significant ($P < 0.001$) with an AGFI of 0.79. As expected, GS was significantly and positively correlated with ITP (0.45; $t=4.02$) and RC was inversely but not significantly correlated with ITP (-0.16; $t=-1.3$) and GS (-0.16; $t=-1.2$). The inverse correlation can be explained by the wording in the negative of the RC response scale. The TSQM domains were highly correlated with GS: with EFF the strongest predictor (0.08; $t=7.6$) followed by CON (0.51; $t=4.8$) and SE (0.47; $t=4.2$). Finally, TCOST (-0.18; $t=-1.3$) and KNO (0.17; $t=1.2$) were correlated with GS, trending in the expected direction. **CONCLUSIONS:** The GS with osteoporosis medication is dependent on effectiveness, side effects, convenience and medication knowledge, and it impacts ITP. Opportunities exist to communicate further information on these treatment attributes to patients to increase GS and ITP. The use of patient-centric methodology in our population yielded expected relationships in a time and cost-efficient manner. A patient-centric study correlating ITP with actual persistence should be explored.

PMS74

PILOT VALIDATION OF THE BRIEF PAIN INVENTORY 'PAIN AT ITS WORST' ITEM IN PATIENTS WITH RHEUMATOID ARTHRITIS

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OBJECTIVES: "Worst pain" intensity has been shown to meaningfully impact patients' lives as indicated by a strong correlation with functional interference scores in rheumatoid arthritis (RA). The objective of this study was to investigate the psychometrics of question 3, 'pain at its worst' of the Brief Pain Inventory Short Form (BPI-sf Q3) in a sample of US patients with self-reported RA. **METHODS:** Fifty adults with RA were recruited to complete questionnaires during an in-person data collection and subsequent one-week at-home mailing. Internal consistency reliability of the BPI-sf pain severity subscale (questions 1-4) was evaluated using Cronbach's α . Test-retest reliability for BPI-sf Q3 was assessed using Intraclass Correlation Coefficient (ICC). Pearson's correlation coefficient was used to assess convergent validity of the BPI-sf Q3 with the Patient Assessment of Arthritis Pain Visual Analogue Scale (VAS). Known-groups discriminant validity was evaluated by comparing BPI-sf Q3 mean scores using analysis of variance of RA severity and general health, and through linear regression for number of bad physical health days. **RESULTS:** Seventy-six percent participants were female, 72% were Caucasian with mean age (SD) 49.4 (13.2) years and mean disease duration 13.7 (12.0) years. The mean score for BPI-sf Q3 was 6.2 (2.4) at the first session and 5.9 (2.2) at retest with ICC 0.79. Correlation with the pain VAS was $r=0.79$ ($p<.001$). Cronbach's α for the severity subscale was 0.94. There was a non-statistically significant relationship between mean BPI-sf Q3 and general health ($p=.22$) and RA severity categories ($p=.12$); and no significant relationship with number of bad physical health days. **CONCLUSIONS:** Assessment of worst pain intensity as measured by the BPI-sf showed validity and reliability in a small sample of patients with RA and may be a useful patient-reported outcome in clinical trials. Further validation in a larger sample is needed to determine known-groups discriminant validity.

Respiratory-Related Disorders – Clinical Outcomes Studies

PRS1

SEVERE ASTHMA EXACERBATIONS ASSOCIATED WITH LONG-ACTING BETA AGONISTS AMONG CHILDREN AND ADOLESCENTS WITH ASTHMA

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OBJECTIVES: The safety of long-acting beta agonists (LABAs) has been in much debate in recent years, resulting from controversial findings reported by various clinical and observational studies with adults. Very limited data on LABA use are available for children and adolescents with asthma. The objective of this study is to assess the risk of severe asthma exacerbations (SAEs) associated with LABA use